

ANSWER 13 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN

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DOCUMENT NUMBER: 143:186315

TITLE: In vitro Procoagulant Activity Induced in Endothelial
Cells by Chemotherapy and Antiangiogenic Drug
Combinations: Modulation by Lower-Dose Chemotherapy

AUTHOR(S): Ma, Li; Francia, Giulio; Vilorio-Petit, Alicia;
Hicklin, Daniel J.; du Manoir, Jeanne; Rak, Janusz;
Kerbel, Robert S.

CORPORATE SOURCE: Molecular and Cellular Biology Research, Sunnybrook
and Women's College Health Sciences Centre and
Department of Medical Biophysics, University of
Toronto, Toronto, ON, Can.

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AB One of the emerging problems concerning the use of antiangiogenic drugs, when used in combination with certain chemotherapy regimens, is enhanced rates and severity of adverse clotting events. For as yet unknown reasons, certain drugs and particular combinations can induce an elevated incidence of thromboembolic events in treated cancer patients [e.g., SU5416, a vascular endothelial cell growth factor receptor-2 (VEGFR-2) antagonist, when combined with gemcitabine and cisplatin (CDDP)]. Such results highlight the need to develop assays capturing the essence of enhanced clot formation under such combination treatment and which may have predictive potential as well. Here, we report the possibility of such an assay (i.e., the ratio of tissue factor over tissue factor pathway inhibitor expression or activity in cultured human endothelial cells calcd. as a coagulation index). A marked increase in coagulation index was obsd. after exposure to SU5416 and the CDDP/gemcitabine chemotherapy combination in contrast to either of these treatments used alone. Substitution of SU5416 with any one of ZD6474, SU6668, IMC-1121, a monoclonal antibody to VEGFR-2, or an antibody to VEGF (Bevacizumab) did not cause a marked increase in the coagulation index, nor did the combination of SU5416 with 5-fluorouracil and leucovorin. Finally, we noted that reducing the concns. of gemcitabine and CDDP (i.e., use of "metronomic dosing" in vitro) significantly attenuated the coagulation index increase induced by these drugs, suggesting that use of low-dose chemotherapy regimens might be an approach to consider for reducing the incidence of adverse clotting events assocd. with chemotherapy alone or in conjunction with antiangiogenic drug combination therapies.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES
AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN TH

ANSWER 4 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2007:561763 CAPLUS
 DOCUMENT NUMBER: 146:494108
 TITLE: Anti-angiogenic activity of 2-methoxyestradiol in
 combination with anti-cancer agents
 INVENTOR(S): Plum, Stacy M.; Strawn, Steven J.; Lavallee, Theresa
 M.; Sidor, Carolyn F.; Fogler, William E.; Treston,
 Anthony M.
 PATENT ASSIGNEE(S): Entremed, Inc., USA
 SOURCE: PCT Int. Appl., 49pp.
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 DOCUMENT TYPE: Patent
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WO 2007059111	A2	20070524	WO 2006-US44152	20061114
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM US 2007185069 A1 20070809 US 2006-599997 20061114 PRIORITY APPLN. INFO.: US 2005-736220P P 20051114 US 2006-788354P P 20060331				

AB The present invention relates generally to methods and compns. of treating disease characterized by abnormal cell proliferation and/or abnormal or undesirable angiogenesis by administering antiangiogenic agents in combination with chemotherapeutic agents. More specifically, the present invention relates to a methods and compns. of treating diseases characterized by abnormal cell proliferation and/or abnormal or undesirable angiogenesis by administering 2-methoxyestradiol, in combination with chemotherapeutic agents.